

Notice of Allowability

Application No.

09/920,332

Examiner

Phuong Huynh

Applicant(s)

KASIBHATLA ET AL.

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1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 5/19/04.
2. ☒ The allowed claim(s) is/are 1,2,4-7,9-13,28-31 and 36-44.
3. ☒ The drawings filed on 02 August 2001 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|---|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date <u>6/21/04</u> . |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.
2. Authorization for this examiner's amendment was given in a telephone interview with Aaron Schwartz on June 21, 2004.
3. **In the claims:**
 1. (currently amended) A method for identifying an immunosuppressive agent comprising:
 - (a) obtaining at least one ~~population~~ sample of viable cultured active T cells having intact cell membranes from a cell growth medium under conditions conducive to growth;
 - (b) combining a first portion of said at least one sample ~~population~~ with a predetermined amount of at least one test compound dissolved in a solvent for a predetermined period of time at a predetermined temperature thereby generating a first volume;
 - (c) combining a second portion of said at least one sample ~~population~~ with an amount of the solvent which was used to dissolve said at least one test compound, for said predetermined period of time at said predetermined temperature thereby generating a second volume;
 - (d) separately adding to each of said first volume and said second volume a cell permeable reporter compound having at least one measurable property which is responsive to the caspase cascade, wherein said reporter compound comprises
 - (i) a caspase substrate; and
 - (ii) a fluorogenic or fluorescent moiety, whereby said at least one measurable property is a change in fluorescence;

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(e) measuring said at least one measurable property of said reporter compound in said first volume and thereby measuring the caspase cascade activity of said first volume;

(f) measuring said at least one measurable property of said reporter compound in said second volume and thereby measuring the caspase cascade activity of said second volume;

(g) calculating a first ratio of caspase cascade activity measured for said first volume to said caspase cascade activity measured for said second volume, wherein when the first ratio is greater than one, said at least one test compound kills active T cells and is identified as a potential immunosuppressive agent.

2. (currently amended) The method of claim 1, further comprising:

(a) obtaining at least one sample population of viable cultured resting T cells having intact cell membranes from a cell growth medium under conditions conducive to growth;

(b) combining said resting T cells with said predetermined amount of said identified immunosuppressive agent dissolved in said solvent for said predetermined period of time at said predetermined temperature thereby generating a third volume;

(c) adding to said third volume said reporter compound having at least one measurable property which is responsive to the caspase cascade;

(d) measuring said at least one measurable property of said reporter compound in said third volume and thereby measuring the caspase cascade activity of said third volume; and,

(e) calculating a second ratio of caspase cascade activity measured for said first volume to said caspase cascade activity measured for said third volume, wherein when the second ratio is greater than one, then said identified immunosuppressive agent is further identified as an active-T-cell-selective immunosuppressive agent.

3. (cancelled)

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4. (Original) The method of claim 1 or 2, wherein said at least one test compound is applied to the T cells at a concentration in the range from about 1 picomolar to about 1 millimolar.

5. (original) The method of claim 1 or 2, further comprising adding a permeabilization enhancer in combination with said reporter compound.

6. (original) The method of claims 1 or 2, wherein said predetermined period of time is about 1 minute to about 48 hours; and wherein said predetermined temperature is about 4°C to about 42°C.

7. (original) The method of claim 6, wherein said predetermined period of time is about 24 hours to about 48 hours.

8. (cancelled)

9. (original) The method of claim 1, wherein a plurality of viable cultured active T cell samples are exposed separately to a plurality of test compounds.

10. (original) The method of claim 2, wherein a plurality of viable cultured resting T cell samples are exposed separately to a plurality of test compounds.

11. (currently amended) The method of claims 9 or 10, wherein said plurality of viable cultured T cell samples cells are in separate wells of a microtiter plate.

12. (original) The method of claim 1, wherein said active T cells are obtained by adding to T cells antibodies to the T cell receptor, Concanavalin A, or Phytohaemagglutinin.

13. (currently amended) The method of claim 2 or 10 ~~claim 1 or 2~~, wherein said active T cells are obtained from tissue of a patient afflicted with one or more immunopathological symptoms and whercin said resting T cells are from healthy tissue that is not afflicted with the immunopathological symptoms.

14.-27. (cancelled)

28. (currently amended) A method for assaying the potency of a test compound to synergise with a known immunosuppressant by functioning as an activator of the caspase cascade, said method comprising:

- (a) obtaining at least one sample ~~population~~ of viable cultured active T cells having intact cell membranes by culturing T cells in a cell growth medium under conditions conducive to growth and activating the cells;
- (b) exposing a first portion of said at least one sample ~~population~~ to a combination of a predetermined amount of said test compound and a subinducing amount of said known immunosuppressant for a first predetermined period of time, at a first predetermined temperature thereby generating a first volume;

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(c) exposing a second portion of said at least one ~~sample population~~ to an amount of solvent which was used to dissolve the test compound and to said subinducing amount of said known immunosuppressant for said first predetermined period of time at said first predetermined temperature thereby generating a second volume;

(d) adding a cell permeable reporter compound to said first volume and to said second volume, said reporter compound having at least one measurable property which is responsive to the caspase cascade, wherein said reporter compound comprises

(i) a caspase substrate; and

(ii) a fluorogenic or fluorescent moiety, whereby said at least one measurable property is a change in fluorescence;

(e) incubating the resulting mixture of said first volume with said reporter compound for a second predetermined time period at a second predetermined temperature;

(f) incubating the resulting mixture of said second volume with said reporter compound for said second predetermined time period at said second predetermined temperature;

(g) measuring said at least one measurable property of said reporter compound in each of said resulting mixtures and thereby measuring the caspase cascade activity of said first volume and of said second volume; and,

(h) calculating the ratio of measured caspase cascade activities of said first volume to said second volume to determine whether said test compound synergises with said known immunosuppressant as an activator of the caspase cascade.

29. (currently amended) The method of claim 28, wherein a plurality of populations of viable cultured active T cell samples cells are exposed separately to a plurality of test compounds.

30. (currently amended) The method of claim 28, wherein said plurality of populations of viable cultured active T cell samples cells are in separate wells of a microtiter plate.

31. (currently amended) A method for identifying an immunosuppressive agent comprising:

(a) obtaining a sample of viable cultured active T cells having an intact cell membrane;

(b) obtaining a sample of viable cultured resting T cells having an intact cell membrane;

(c) separately exposing the active and resting T cell samples cells to at least one test compound for a predetermined period of time under predetermined conditions;

(d) adding a cell permeable reporter compound having at least one measurable property which is responsive to the caspase cascade to the active and resting T cells that have been exposed to the at least one test compound, wherein said reporter compound comprises

(i) a caspase substrate; and

(ii) a fluorogenic or fluorescent moiety, whereby said at least one measurable property is a change in fluorescence;

(e) measuring the caspase cascade activity in the active T cells exposed to the at least one test compound by measuring said at least one measurable property; and

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(f) measuring the caspase cascade activity in said resting T cells exposed to the at least one test compound by measuring said at least one measurable property, wherein when the caspase cascade activity in the active T cells is greater than the caspase cascade activity in the resting T cells, the at least one test compound selectively kills active T cells and is an immunosuppressive agent.

32.-35. (cancelled)

36. (previously presented) The method of claim 28 or 31, wherein said at least one test compound is applied to the T cells at a concentration in the range from about 1 picomolar to about 1 millimolar.

37. (previously presented) The method of claim 28 or 31, further comprising adding a permeabilization enhancer in combination with said reporter compound.

38. (previously presented) The method of claims 28 or 31, wherein said predetermined period of time is about 1 minute to about 48 hours; and wherein said predetermined temperature is about 4°C to about 42°C.

39. (previously presented) The method of claim 38, wherein said predetermined period of time is about 24 hours to about 48 hours.

40. (previously presented) The method of claim 31, wherein a plurality of viable cultured active T cell samples are exposed separately to a plurality of test compounds.

41. (previously presented) The method of claim 31, wherein a plurality of viable cultured resting T cell samples are exposed separately to a plurality of test compounds.

42. (previously presented) The method of claims 40 or 41, wherein said plurality of viable cultured cells are in separate wells of a microtiter plate.

43. (previously presented) The method of claim 28 or 31, wherein said active T cells are obtained by adding to T cells antibodies to the T cell receptor, Concanavalin A, or Phytohemagglutinin.

44. (currently amended) The method of claim 31 or 41 ~~claim 28 or 31~~, wherein said active T cells are obtained from tissue of a patient afflicted with one or more immunopathological symptoms and wherein said resting T cells are from healthy tissue that is not afflicted with the immunopathological symptoms.

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REASONS FOR ALLOWANCE

4. The following is an examiner's statement of reasons for allowance:
5. Claims 1, 2, 4-7, 9-13, 28-31 and 36-44 are pending.
6. The rejections under U.S.C 103(a) are hereby withdrawn in view of the statement filed on 5/19/04 by Robert W. Esmond that the ownership of the present application and the '611 patent were, at the time the present invention was made, owned by, or subject to an obligation of assignment to the same person.
7. Claims 1, 2, 4-7, 9-13, 28-31 and 36-44 are allowed.
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.
9. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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June 23, 2004


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